REMARKS AND RESPONSE TO RESTRICTION REQUIREMENT

Claims 1, 3-8, and 21-30 are pending in the application.

Election/Restrictions

In Applicant's response filed March 11, 2008, the claims were amended to read on multiple combinations of genes, which are now subject to a restriction requirement. The Office Action of May 30, 2008 requested Applicants to "...elect a single combination of specific genes used for the method of diagnosis of renal cell carcinoma in a human." The Office Action also requested the selection of the specific SEQ ID NOs in the selected combination of renal cell carcinoma genes. (See page 2 of the Office Action.)

The Office Action asserted that each method of using a single combination of different genes constituted an Invention Group. It was alleged that: 1) the inventions as claimed, are either not capable of use together, or can have a materially different function or effect; 2) the different inventions will produce different results; and 3) the different genes would not share the same core structure, and would have different properties and therefore different functions. (See page 3 of the Office Action.)

In response to the restriction requirement, Applicants provisionally elect, with traverse, the combination of eukaryotic elongation factor 1 alpha 2 (EEF1A) and toll-like receptor 2 (TLR2). EEF1A corresponds to SEQ ID NO:285, and TLR2 corresponds to SEQ ID NOs: 1 and 240.

The claims recite a method for diagnosis of RCC in a sample comprising comparing the expression profile of two or more RCC genes to at least one reference expression profile, wherein differential expression of the two or more RCC genes is indicative of the presence or absence of RCC. Claim 1 recites twenty genes that are differentially expressed in RCC samples as compared to disease-free samples.

Applicants respectfully traverse the restriction requirement and submit that the restriction is improper because the inventions are related for at least the following:

1) The genes are capable of use together

Applicants submit that each method of using a combination of two or more of the genes listed in the claims yields the same effect, i.e. the indication of the presence or absence of RCC. This is contrary to the assertions proffered in the Office Action. Applicants respectfully submit that the genes listed in the claims are capable of use together and the methods of the claims are useful in the diagnosis of RCC, i.e. the indication of the presence or absence of RCC.

2) The different genes will produce the same result

Contrary to the assertions of the Office Action, use of the different genes as mentioned in the claims will produce the same result. The invention comprises different sub combinations of a group of genes in a method directed to the same process, i.e. indicating the presence or absence of RCC.

The Office Action asserts that each single combination of specific genes used for the method constitutes a different invention that will produce a different result. Applicants submit, however, that each method of using a single combination or two or more of the genes listed in the claims will produce the same result, i.e., an indication of either the presence or absence of RCC.

3) The different genes have the same functions

The Office Action further asserts that the different genes do not share the same core structure, and alleges that the different genes would have different properties, and therefore would have different functions. However, the claims recite a defined set of genes that utilize a common property to obtain a desired result. Contrary to the Office Actions assertions, the specification as filed teaches that the genes listed in the claims are differentially expressed in RCC samples as compared to disease-free samples (see, for example, Table 8 of the specification as filed). Differential expression of the genes in RCC samples as compared to disease-free samples is an indication of RCC, the claimed function. The fact that the core structures of the genes differ is not relevant to their claimed use of diagnosing RCC.

Accordingly, contrary to the assertions of the Office Action, the recited methods of using a combination of two or more of the genes for diagnosis of RCC as listed in the claims, are 1) capable of use together, 2) will produce the same results; and 3) the different genes have the same function.

Furthermore, according to MPEP § 803, there are two criteria for a restriction requirement to be proper. "A) the inventions must be independent or distinct as claimed; and B) there would be a serious burden on the examiner if restriction is not required."

Applicants respectfully submit that the methods of using the different combinations of genes to diagnose RCC as claimed are related because they are disclosed in the specification as enabling diagnosis of RCC. The different combinations of genes are used in the same process, i.e. to diagnose RCC. The different combinations of genes, as listed in the claims, do not meet the requirements of "related but distinct" as defined in the MPEP § 802.01 II (emphasis added):

> "Two or more inventions are related (i.e., not independent) if they are disclosed as connected in at least one of design (e.g., structure or method

> of manufacture), operation (e.g., function or method of use), or effect. Examples of related inventions include combination and part (subcombination) thereof, process and apparatus for its practice, process and product made, etc. In this definition the term related is used as an alternative for dependent in referring to inventions other than independent inventions.
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> Related inventions are distinct if the inventions *as claimed* are not connected in at least one of design, operation, or effect (e.g., can be made by, or used in, a materially different process) and wherein at least one invention is PATENTABLE (novel and nonobvious) OVER THE OTHER (though they may each be unpatentable over the prior art). See MPEP § 806.05(c) (combination and subcombination) and § 806.05(j) (related products or related processes) for examples of when a two-way test is required for distinctness."

All twenty genes recited in the claims are differentially expressed in RCC tissue as compared to disease-free tissue. Each combination of genes is to be used for the same material process, namely to diagnose RCC by comparing the expression profile of two or more of the RCC genes recited in the claims to at least one reference expression profile, wherein differential expression of the two or more RCC genes is indicative of the presence or absence of RCC.

All twenty genes are differentially expressed in RCC patients as compared to disease-free humans, as indicated in Table 8 of the instant application. This differential expression allows the use of the different combinations of genes for their function in the claimed relationship, i.e. to diagnose RCC. Thus, all 20 genes can be used in the same process, to diagnose RCC.

Moreover, according to MPEP § 803.02, it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common, which is mainly responsible for their function in the claimed relationship. All 20 genes recited in claim 1 are disclosed in the specification to possess at least one property in common, these genes are disclosed in the specification as being differentially expressed in RCC tissue as compared to disease-free tissue. This property is mainly responsible for their function in diagnosing RCC. The different combinations of genes are used in the claims to diagnose RCC. According to the MPEP § 803.02:

> "...However, it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is mainly responsible for their function in the claimed relationship, and it is clear from their very nature or from the prior art that all of them possess this property..."

In summary, Applicants submit that the restriction requirement is not proper because all the genes listed in the claims possess at least one property in common. All twenty genes listed in the claims are differentially expressed in RCC samples as compared to disease free

samples. The common property of these genes is the fact that these genes are differentially expressed in RCC samples as compared to disease free samples. As such, this common property identified by the Applicant is mainly responsible for their function in the claimed relationship, i.e., diagnosing RCC.

Species Election

At page 4, the Office Action requests the election of a single ultimate species for a first gene and a second gene. According to the Office Action, "the species are independent because claims to the different species recite the mutually exclusive characteristics of such species." (See page 4 of the Office Action.)

In response to the species election requirement, Applicants elect, TLR2 as the first specific gene and EEF1A2 as the second specific gene for the minimum combination of two genes.

Furthermore, Applicants respectfully request that should the above-named combination be allowable the rest of the combinations be examined. MPEP § 821.04 states that the propriety of a restriction requirement should be reconsidered when all the claims directed to the elected invention are in condition for allowance:

> **>The propriety of a restriction requirement should be reconsidered when all the claims directed to the elected invention are in condition for allowance, and the nonelected invention(s) should be considered for rejoinder. Rejoinder involves withdrawal of a restriction requirement between an allowable elected invention and a nonelected invention and examination of the formerly nonelected invention on the merits.

The examiner is invited to contact the undersigned Agent to discuss any outstanding issues. Early and favorable action on the merits is respectfully requested.

During the pendency of this application please treat any reply requiring a petition for extension of time for its timely submission as containing a request therefore for the appropriate length of time. The Commissioner is hereby authorized to charge all required extension of time fees during the entire pendency of this application to Deposit Account No. 01-1425.

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